

data were not corrected for the intensity variation of the phantoms. The kidneys enhanced an average of 34% over 90 minutes, reaching a maximum of 45% enhancement at about 30 minutes. The liver enhanced an average of about 20% over 90 minutes, reaching a maximum of about 23% at about 5 to 40 minutes. FIG. 27 shows the ratio of enhancement, relative to precontrast enhancement, of the kidneys to liver, showing the time course of enhancement of these two organs to be similar, indicating that the enhancement agent was not selectively eliminated by either of these organs during the 90 minute experimental time period. This indicates recirculation of the enhancement agent in the blood pool of the rats.

This Example illustrates that the enhancement seen in the liver and kidneys, both highly vascularized organs, is easily visible even at a dose of 0.015 mmol Gd^{+3} /kg, one tenth the normal clinical dose of Gd-diethylenetriamine pentaacetic acid for magnetic resonance imaging. The high magnetic resonance sensitivity of the paramagnetic polymerized lipid preparation results from: (1) The particulate nature of the polymerized lipid slows the correlation time for reorientation of the Gd^{+3} ion, which concentrates the power of the relaxation-affecting magnetic fluctuations in the regime of the water proton Larmor frequency and results in a higher molar relaxivity per Gd^{+3} ion of $11.2 \text{ mM}^{-1}\text{s}^{-1}$, as compared with Gd-diethylenetriamine pentaacetic acid of $4.2 \text{ mM}^{-1}\text{s}^{-1}$; and (2) The paramagnetic polymerized lipid particles are confined to the blood pool and do not leak into the interstitial spaces, as does Gd-diethylenetriamine pentaacetic acid. The reduced volume of distribution leads to a relatively increased blood pool concentration of gadolinium for the paramagnetic polymerized liposomes, as compared to a similar body weight dosage of Gd-diethylenetriamine pentaacetic acid.

Extended recirculation of the paramagnetic polymerized liposomes and their lack or absence of retention by the kidneys and liver is evident from the prolonged magnetic resonance intensity enhancement and the constant ratio of enhancement for these organs, as compared to Gd-diethylenetriamine pentaacetic acid, which is eliminated from the blood pool within a few minutes. The prolonged recirculation of the paramagnetic polymerized liposomes results from reduction in phagocytosis by macrophages of the reticuloendothelial system by selection and control of the particle size and, perhaps, by use of polyethylene linkers for attachment of the Gd^{+3} ion. Evasion of the reticuloendothelial system is probably complemented by evasion of the immune system by use of phosphatidyl choline, which is the major component of mammalian cells, as the matrix for presentation of the paramagnetic and ligand-bearing paramagnetic polymerized liposomes of this invention.

While in the foregoing specification this invention has been described in relation to certain preferred embodiments thereof, and many details have been set forth for purpose of illustration it will be apparent to those skilled in the art that the invention is susceptible to additional embodiments and that certain of the details described herein can be varied considerably without departing from the basic principles of the invention.

We claim:

1. A polymerized liposome image contrast agent composition consisting essentially of: liposome forming lipids, said liposome forming lipids having active hydrophilic head groups selected from the group consisting of diethylenetriamine pentaacetic acid, ethylenedinitrile tetraacetic acid, tetraazacyclododecane 1,4,7,10-tetraacetic acid, and cyclohexane- 1,2,-diamino-N,N'-diacetate, said active hydrophilic head groups having functional surface groups chelated

with an image contrast enhancement agent; said liposome forming lipids having hydrophobic tail groups polymerized with a hydrophobic tail group of an adjacent said liposome forming lipid through a functional group selected from the group consisting of diacetylene, olefin, acetylene nitrile, styrene, ester, thiol, amide, α , β unsaturated ketone, and α , β unsaturated aldehyde; said hydrophilic head groups and said hydrophobic tail groups linked to said liposome forming lipid by a variable length linker portion selected from the group consisting of variable length polyethylene glycol, polypropylene glycol and polyglycine.

2. A polymerized liposome image contrast agent composition according to claim 1 wherein said active hydrophilic head group is diethylenetriamine pentaacetic acid and said hydrophobic tail group is diacetylene.

3. A polymerized liposome image contrast agent composition according to claim 1 wherein said active head group is diethylenetriamine pentaacetic acid-bis(10,12-pentacosadiynoic amide) lanthanide ion chelator and said hydrophobic tail group is diacetylene.

4. A polymerized liposome image contrast agent composition according to claim 1 wherein said image contrast enhancement agent is selected from the group consisting of Gd^{3+} , Dy^{3+} , Tc and In

5. A polymerized liposome image contrast agent composition according to claim i wherein said hydrophilic head group comprises a lanthanide-diethylenetriamine pentaacetic acid chelate.

6. A polymerized liposome image contrast agent composition consisting essentially of: liposome forming lipids, said liposome forming lipids having active hydrophilic head groups selected from the group consisting of diethylenetriamine pentaacetic acid, ethylenedinitrile tetraacetic acid, tetraazacyclododecane 1,4,7,10-tetraacetic acid, and cyclohexane- 1,2,-diamino-N,N'-diacetate, a portion of said active hydrophilic head groups having functional surface groups chelated with an image contrast enhancement agent and additional said active hydrophilic head groups having attached targeting active agents; said liposome forming lipids having hydrophobic tail groups polymerized with a hydrophobic tail group of an adjacent said liposome forming lipid through a functional group selected from the group consisting of diacetylene, olefin, acetylene, nitrile, styrene, ester, thiol, amide, α , β unsaturated ketone, and α , β unsaturated aldehyde; said hydrophilic head groups and said hydrophobic tail groups linked to said liposome forming lipid by a variable length linker portion selected from the group consisting of variable length polyethylene glycol, polypropylene glycol and polyglycine.

7. A polymerized liposome image contrast agent composition according to claim 6 wherein said additional hydrophilic head groups are selected from the group consisting of biotin, amine, carboxylic acid and isothiocyanate.

8. A polymerized liposome contrast agent composition according to claim 6 wherein said targeting active agent is a ligand.

9. A polymerized liposome image contrast agent composition according to claim 6 wherein said image contrast enhancement agent is selected from the group consisting of Gd^{3+} , Dy^{3+} , Tc and In.

10. A polymerized liposome image contrast agent composition according to claim 6 wherein said hydrophilic head group comprises a lanthanide-diethylenetriamine pentaacetic acid chelate.

11. A polymerized liposome image contrast agent composition according to claim 6 wherein said active hydrophilic head group is diethylenetriamine pentaacetic acid and said hydrophobic tail group is diacetylene.